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Specification and Drawings, as originally filed, with Application for Patent Serial No: **2,433,205,** on June 25, 2003, by **JAMES ALEXANDER KEENAN,** for "Drug Delivery, Bodily Fluid Drainage, and Biopsy Device with Enhanced Ultrasonic Visibility".

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ABSTRACT

A medical device to inject drugs, drain bodily fluids, or to perform biopsy is disclosed. The device will permit localized drug delivery, fluid drainage, or biopsy through real-time monitoring of the needle tip position within a patient. The device will permit controlled dispersion of a drug into solid tissue as well as delivery into specific blood vessels.

As a needle is inserted an echogenic fluid, such as a saline solution or an ultrasound contrast agent, is injected into the patient. The fluid travels a brief distance before being slowed and stopped by the patient's tissue. This fluid flow will be detectable by ultrasound, likely Doppler ultrasound.

The position of the needle tip during insertion will be monitored using an ultrasound until it is positioned at the desired point of action. A therapeutic drug is then delivered. Alternatively, a vacuum pump could then be used to aspirate fluid for drainage or tissue for biopsy.

During needle insertion, the fluid flow rate may be adjusted to vary the volume of space detectable by the ultrasound so as to maintain a properly defined image of the needle tip.

Once the needle tip is positioned at the point of action, the echogenic fluid can be pulsed, repeatedly and at a variety of flow rates, until the fluid distribution pattern is satisfactory and the drug can then be delivered.

TITLE: Drug Delivery, Bodily Fluid Drainage, and Biopsy Device with Enhanced Ultrasonic Visibility

FIELD OF THE INVENTION

The invention pertains to ultrasonic guidance of the position of the distal tip of a needle within a patient. The device can be used to inject therapeutic agents, drain bodily fluids, or to perform biopsy. The device can be used to control the dispersion of a therapeutic agent into solid tissue as well as to deliver a therapeutic agent into specific blood vessels.

BACKGROUND TO THE INVENTION

Medical Rationale

Accurate, real-time knowledge of a needle tip location is an obvious requirement of a biopsy procedure. It is also desired in order to deliver drugs to a specific target site as well as to avoid puncture damage to other tissue. Biotherapeutics, which are expected to comprise more than half of the new drugs developed in the next two decades, are often large molecules that degrade rapidly in the bloodstream and have a limited ability to cross cell membranes. Oral and intravenous delivery techniques may prove inadequate, and some biotherapeutics may require localized injection delivery.

Localized drug delivery permits a higher concentration of a therapeutic agent at the target site while minimizing side effects, as in the case of cytotoxic chemotherapy drugs. Localized delivery also results in a reduction of the required

dosage amount and therefore cost, which is of benefit for applications such as gene therapy.

Intratumoral injections, such as ablation of liver tumors through alcohol injection, require precise needle positioning and fluid delivery.

Anti-angiogenics are drugs designed to damage tumours by attacking the blood vessels that feed them. A device that permits the delivery of a drug to a particular blood vessel could enhance its efficacy. Potentially, a method to clot the artery feeding a tumor could be used.

Acoustically active drug delivery systems, such as described in United States Patent 6,416,740 for Bristol-Myers Squibb Imaging, consist of gas filled microspheres that, under external ultrasound, rupture to release a therapeutic compound in a specific region of the body. Although designed for intravenous delivery, this system may show enhanced efficacy if delivered via needle and a transducer mounted in the syringe delivered the rupturing ultrasound pulse down through the needle.

Ultrasound Imaging

Ultrasound is a standard technique to image the internal body for diagnoses, and these images are usually displayed on a monitor in grey-scale. Doppler ultrasound techniques (color Doppler sonography, pulsed Doppler ultrasound, continuous wave CW Doppler, and power Doppler sonography) are typically used to measure or image blood flow. The ultrasound signal bounces off of the moving blood cells and returns to the transducer,

with the returning echo shifted in pitch by the Doppler effect. The moving objects can be assigned a color so that they appear in color against a grey-scale background, such as a patient's internal organs.

Doppler ultrasounds detect the motion of red blood cells, which are bioconcave discs about 7.5 micrometers in diameter and which comprise 40 to 45 percent of the blood. Color Doppler ultrasounds can detect displacements as low as microns (1 micron = 0.001 millimeter) and at speeds in the 1 to 100 centimeters per second range.

Ultrasound Imaging of Needles

Smooth, thin needles are difficult to perceive in ultrasound output image unless the ultrasound pulses approach the needle at close to ninety degrees. Core biopsy needles are typically 14 to 18 gauge while needles for drug injection range from 18 to 26 gauge or beyond.

Patents to enhance the ultrasonic visibility of needle tips have been granted. One approach is to roughen or groove the needle tip but this may increase the trauma of needle insertion.

Other approaches to enhance ultrasound visibility include: producing bubbles at the needle tip to better reflect ultrasound, mounting miniature transducers at the needle tip, vibrating a solid stylet carried coaxially within a hollow biopsy needle, reciprocating a stylet longitudinally using a solenoid coil in the syringe, and using transducers to

generate a longitudinal oscillation of a fluid column coupled to the needle tip. A difficulty encountered by some of these approaches is that motion was not confined to the needle tip and the Doppler ultrasound colored the entire needle. An invention that featured a loudspeaker connected to a hollow stylet was successful in displaying the needle tip as a color beacon regardless of the angle of incidence of the Doppler beam, but tissue material could block the needle during insertion and stop the color signal at the tip.

Syringes and Syringe Pumps

Injecting fluid into a patient with sufficient speed and duration to be detectable by ultrasound can be accomplished with a standard syringe and the force of a person's thumb. However, it is difficult to consistently control the fluid flow manually in order to precisely locate the position of the needle tip using ultrasound.

The concept of injecting two fluids using one syringe is not novel. Double barreled syringes are commercially available for medical uses and for mixing epoxy. US patent 6,245,046 discloses a syringe with thumb control for fluid delivery and aspiration. These inventions do not claim enhanced ultrasonic visibility.

Microprocessor controlled, automated syringe pumps are established technology. Commercial manufacturers include Fisher Scientific for laboratory applications, insulin pumps from Animas Corporation, and intravenous infusion pumps from Baxter.

US patent 6,423,035, by Das, et al., 'Infusion pump with a sealed drive mechanism and improved method of occlusion detection' states:

"The infusion pump includes processing circuitry for controlling the drive mechanism to infuse medication to a patient, including a sensor to track the position of the syringe plunger... An infusion pump for dispensing volumetrically proportioned doses of pharmaceutical product to a subject by way of an infusion path, the infusion path being adapted to connect the pump intravenously or subcutaneously to the subject..."

US patent 6,423,035 did not claim the ejection of fluid into solid tissue as a needle is inserted into a patient in order to enhance the ultrasonic visibility of the needle tip, the controlled dispersion of a drug into solid tissue, or the delivery of a drug into a blood vessel by precise positioning of a needle tip.

Fluid Pressure Monitoring of Medical Devices

The concept of a syringe pump with continuous pressure monitoring and display to detect occlusions has been disclosed, in US patent 5,295,967, by Rondelet, et al. However, this is an infusion therapy device intended to deliver drugs intravenously. This patent did not claim the ejection of fluid continuously into solid tissue as a needle is inserted into a patient in order to enhance the ultrasonic visibility of the needle tip.

Using pressure to precisely locate the distal end of a delivery tube was disclosed in US patent 6,251,079, by Gambale, et al, in 'Transthoracic drug delivery device'. However, that invention comprised a pressure sensing tube mounted in parallel to a drug delivery tube to provide transthoracic drug delivery, in particular for therapeutic substances to be ejected into the myocardium.

Ultrasound Contrast Agents

Ultrasound contrast agents are commercially available from companies such as Bristol-Myers Squibb and Amersham. Contrast agents are echogenic and are intended to produce optimum ultrasound wave reflection in order to improve the received image relative to the surrounding tissue. This permits improved visualization of blood flow.

An Amersham product, Optison, consists of a suspension of human albumin microspheres with acoustic properties that cause them to produce ultrasound wave backscatter. Optison is administered intravenously in dose sizes from 0.5- to 1.0-mL, up to 8.7 mL. The microspheres have a mean diameter of between 2.0 and 4.5 μm - smaller than red blood cells. Optison enhances the image of the endocardial borders of the heart to allow doctors to see abnormalities in the walls of the heart.

Fluid Conditioning of Tissue

Methods to condition tissue in order to facilitate drug delivery have been developed or studied.

Needleless injection devices force liquids through the skin at speeds up to 400 meters/second using compressed gas. From US Patent 6,319,224 'Intradermal injection system for injecting DNA-based injectables into humans', from Stout et al.: "Pressurizing a liquid injectable within an ampule...to...3900-4300 psi, within 5 milliseconds... causing local tissue disruption within the intradermal space... thereby encouraging an immune response...."

Tachibana et al, Fukuoka University School of Medicine, describe another method in 'Targeted Drug Delivery with Microbubble': "Microbubbles can be intentionally ruptured...to promote diffusion of drugs into various tissues and lesions. It has been demonstrated that microbubbles and ultrasound can markedly accelerate penetration of lytic agents into thrombus."

These methods suggest the potential benefit of fluid pulses, with precisely controlled flow rates and flow volumes, that could condition tissue prior to the injecting a therapeutic agent.

SUMMARY OF THE INVENTION

A medical device to inject drugs, drain bodily fluids, or to perform biopsy is disclosed. The device will permit localized drug delivery, fluid drainage, or biopsy through real-time monitoring of the needle tip position within a patient. The device will permit controlled dispersion of a therapeutic

agent into solid tissue as well as drug delivery into specific blood vessels.

The device is comprised of a handheld assembly with a needle, needle adapter, vessels to contain two different fluids, fluid conduit, fluid pump, controls, pressure sensor, flow sensor, fluid switching mechanism, and valve as shown in figures 1, 2, 3, 3A, and 4. An alternative embodiment of the invention shown in figure 6 depicts one or both fluid vessels connected to the hand held assembly via flexible fluid conduit. The handheld assembly is connected to a flow meter, pressure meter, controller, controller I/O, flow rate and pressure display, and power source as shown in figures 1 and 2. The device is depicted as used for drug delivery in figure 1 and biopsy in figure 2, where a vacuum source and conduit is also depicted.

In a preferred embodiment of the invention as shown in figures 3, 3A and 4, the fluid vessels are syringes with plungers and the pump is a syringe pump.

As the needle is inserted, the first fluid, possibly an ultrasonic contrast agent, is injected into the patient. The fluid travels a brief distance before being slowed and stopped by the patient's tissue. This speed and travel distance will be of sufficient magnitude as to be detectable by ultrasound, likely Doppler ultrasound, which is commonly used to image blood flow. A wide range of fluid speed and travel distance would be acceptable: 1 cm/sec up to 100 m/sec and 10 microns up to 5 mm.

The patient's internal organs can be displayed in grey-scale while the Doppler ultrasound assigns a distinct color to the fluid flow at the needle tip.

The health care personnel will monitor the position of the needle tip during insertion until said tip is positioned at the desired point of action, for instance a particular organ or a cancer tumor. The second fluid, likely a therapeutic drug, is then delivered. Alternatively, a vacuum pump could then be used to aspirate tissue for biopsy or fluid for drainage.

During needle insertion, the first fluid may be pumped continuously or intermittently using the manual controls, or pulsed using the processor. The health care personnel will monitor the needle tip position through an ultrasound display and may adjust the fluid flow rate. This will vary the volume of space detectable by the ultrasound so as to maintain a properly defined image of the needle tip.

If too high a fluid flow rate is ejected during the needle insertion it would tend to disrupt tissue and the fluid distribution would be unpredictable. The fluid could flow for centimeters in multiple directions and too large a volume of space would be detected by the ultrasound to permit precise monitoring of the needle tip. Minute adjustments of the flow rate will likely be required in order to contain the zone of flowing fluid to a small volume of space in proximity to the needle tip. Therefore the motor RPM range, gear ratio between the motor link, drive shaft and syringe plunger actuator links, the motor driver card, and the automatic controls must

be specified to provide sufficient control to provide minute, real-time adjustments to the flow rate.

The device can be used to precisely control the delivered volume of the drug, using the controller, flow meter, and pump.

The device can also be used to precisely control the dispersion pattern of a delivered drug. Once the needle tip is positioned at the point of action, the health care personnel can pulse the echogenic fluid, repeatedly and at a variety of flow rates if necessary, and monitor the fluid distribution pattern. The flow rates of these preliminary fluid pulses can be high enough to condition the tissue at the point of action which may benefit the drug distribution. Once the dispersion pattern is satisfactory, the second fluid, the therapeutic agent, can then be delivered.

There are a number of options for Fluid 1, the echogenic fluid to be ejected during the needle insertion. The key requirements are that Fluid 1 be biologically harmless (such as sterile saline), incompressible, and echogenic. Fluid 1 must have no adverse effect on Fluid 2, the therapeutic agent, as the needle and fluid conduits will not be flushed between injections of the two fluids. A suspension, and in particular an echo contrast agent, would be the preferred choice. Fluid 1 could contain drugs that aided the efficacy of the therapeutic agent, such as a drug to prevent infection or to aid or to combat the migration of the therapeutic agent. It could also contain a chemical additive to decrease its viscosity. Fluid 1 could even be the patient's own blood,

reused as per a transfusion. Fluid 1 could be an echogenic gas.

Fluid 2, the therapeutic agent delivered at the point of action, could be: a liquid drug, solid drug particles suspended in a fluid, drug eluting microspheres suspended in a fluid, or other therapeutic agents that can be delivered under pressure through a needle. Likely, a small quantity of the therapeutic agent, 0.2 to 1.0 ml, will be delivered.

The device may display the flow rate, fluid pressure, and the rate of change of the pressure to the attending health care personnel. For biopsy or fluid drainage use, the device will also display the vacuum.

The pressure required to maintain a constant flow rate will vary as the back pressure varies due to the depth of needle insertion and changes in density of the patient's tissue, i.e. as the needle tip passes from fat to muscle. The back pressure may drop sharply if the needle tip pierces a blood vessel wall and the echogenic fluid is ejected directly into an artery or vein. Therefore, by monitoring the pressure and rate of change of the pressure, the health care personnel will be able to position the needle to deliver drugs directly into a particular blood vessel. If required, an auditory or visual alarm could be incorporated into the system to alert attending health care physicians when the pump pressure has dropped sharply and the needle tip has pierced a blood vessel wall.

The syringe pump as depicted in figures 3, 3A, and 4 is comprised of: an electric stepper motor, a drive shaft,

linkages to connect said motor to the drive shaft and the shaft to the syringe plunger actuators.

An alternate embodiment of the invention, as depicted in figures 5A and 5B, uses a mechanical mechanism to transfer the fluid.

Another alternative embodiment of the invention, as depicted in figure 6, consists of an adapter to a commercial intravenous infusion pump. The hand held assembly is used to insert the needle and to control the infusion pump that transfers the fluid.

The foregoing summarizes the principal features of the invention and some of its optional aspects. The invention may be further understood by the description of the preferred embodiments, in conjunction with the drawings, which now follow.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 depicts an embodiment of the invention being used to deliver drugs.

Figure 2 depicts an embodiment of the invention being used to perform biopsy.

Figure 3 depicts a side view of the hand held assembly with the therapeutic agent (not shown) and ultrasonic contrast agent contained in syringes with plungers.

Figure 3A depicts a top view of the fluid flow and mechanical drive of the hand held assembly in the embodiment with the

therapeutic agent and ultrasonic contrast agent contained in syringes.

Figure 4 depicts an isometric view of the switch mechanism and mechanical drive portion of the hand held assembly, configured to deliver drugs.

Figures 5A and 5B depict top and side views of an embodiment of the invention using a mechanical mechanism to transfer the fluid.

Figure 6 depicts an embodiment of the invention consisting of a hand held adapter connected to a commercial intravenous infusion pump.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Figure 1 depicts the device being used to perform localized drug delivery at a depth within a patient.

An ultrasound transducer (1) transmits and receives pulses in order to image the interior of a patient (2) on an ultrasound display (3). The hand held assembly (5) is used to insert a needle (6) into the patient towards the desired point of action (4), an organ, tumor, etcetera. The distal tip of the needle (7) ejects fluid at sufficient speed and for sufficient travel distance as to be detectable by the ultrasound.

A flow meter sensor (8) mounted on the distal end of the hand held assembly (5) is connected to the flow meter (9). A pressure sensor (10) mounted on the distal end of the hand held assembly (5) is connected to the pressure meter (11). Trigger controls (12) and (13) enable the health care personnel to switch the flow on/off and to adjust the flow

rate.

The controller (14) is a microprocessor connected via a wire wrap cable (27), to the manual controls, power source and driver (15), flow meter (9), pressure meter (11), input/output (17), and the flow meter/pump pressure display (18). The controller input/output (17) enables the health care personnel to enter commands to specify pulsed flow etcetera.

The power source and driver (15) drives the syringe pump motor (16), which is linked to a drive shaft (not shown), that actuates the plunger (20) for the syringe containing the ultrasonic contrast agent (19).

Once the needle tip (7) is positioned at the desired point of action (4), the health care personnel stop the flow of Fluid 1 and inject Fluid 2, the therapeutic drug (syringe not shown) into the patient (2).

The fluid flow is switched using a manual switching mechanism (23) connected to a push button (22). The switching mechanism (23) simultaneously engages/disengages the syringe plunger actuators from one syringe to the other as well as switching the fluid valve (21) from one syringe to the other.

Figure 2 depicts the device being used to perform biopsy at a depth within a patient.

An ultrasound transducer (1) transmits and receives pulses in order to image the interior of a patient (2) on an ultrasound display (3). The hand held assembly (5) is used to insert a

needle (6) into the patient towards the desired point of action (4), an organ, tumor, etcetera. The distal tip of the needle (7) ejects fluid at sufficient speed and for sufficient travel distance as to be detectable by the ultrasound.

A flow meter sensor (8) mounted on the distal end of the hand held assembly (5) is connected to the flow meter (9). A pressure sensor (10) mounted on the distal end of the hand held assembly (5) is connected to the pressure meter (11). Trigger controls (12) and (13) enable the health care personnel to switch the flow on/off and to adjust the flow rate.

The controller (14) is a microprocessor connected via a wire wrap cable (27), to the manual controls, power source and driver (15), flow meter (9), pressure meter (11), input/output (17), vacuum source (33), valve (32), and the flow meter/pump pressure/vacuum display (18). The controller input/output (17) enables the health care personnel to enter commands to specify pulsed flow etcetera. The vacuum source (33) is connected to the hand held assembly (5) with a vacuum line (34).

The power source and driver (15) drives the syringe pump motor (16), which is linked to a drive shaft (not shown). The drive shaft drives the plunger actuator (29), which slides along support rods (31) to actuate the plunger (20) for the syringe containing the ultrasonic contrast agent (19).

Once the needle tip (7) is positioned at the desired point of action (4), the health care personnel stop the fluid flow and

close the valve (32). The vacuum source (33) is then used to aspirate tissue for biopsy.

Figure 3 depicts the hand held assembly of the device configured to deliver drugs.

A hand held assembly (5) with a needle adaptor (26) to hold a needle (6) for injecting drugs to a depth within a patient is shown. A sensor (8)detects the fluid flow rate. A pressure sensor (10) detects the fluid pressure. A top trigger control (12) with a position sensor (24) is used to set the flow rate and a lower trigger (13) and switch (25) is used to switch the flow on and off. The flow sensor (8), pressure sensor (10), top trigger position sensor (24), and lower trigger switch (25) are connected via a wire wrap cable (27), which runs out to the flow meter, pressure meter, and controller.

The power source and driver card (not shown) is connected via wire (28) to the syringe pump motor (16), which is mechanically linked (39) to a drive shaft (not shown). Alternatively, the pump motor may be battery driven (not shown). The drive shaft is linked to the plunger actuator (29) which slides along the horizontal support rods of the switching mechanism (23) to actuate the plunger (20) for the syringe containing the ultrasonic contrast agent (19). This syringe (19) is fastened to the switching mechanism (23) through an adjustable syringe clamp (30).

During insertion of the needle (6) into the patient, the plunger (20) is actuated, and Fluid 1 flows from the syringe, through a fluid valve (21), a fluid conduit (42), and through

the needle (6) where it is injected into the patient.

Once the needle tip is positioned at the desired point of action the flow of Fluid 1, the ultrasound contrast agent, is stopped to permit flow from Fluid 2, the therapeutic agent, (syringe not shown). The fluid flow is switched by actuating a push button (22) connected to the switching mechanism (23). The switching mechanism (23) simultaneously engages/disengages the syringe plunger actuators from one syringe to the other as well as switching the fluid valve (21) from one syringe to the other.

Figure 3A depicts a top view of fluid flow and mechanical drive portion of the hand held assembly, configured to deliver drugs.

The syringe pump motor (16) is mechanically linked (39), to a drive shaft (37), which is supported by two bearings (38). The drive shaft is mechanically linked (40) to either syringe plunger actuator (29), which slide parallel to the drive shaft along the horizontal support rods of the switching mechanism (not shown). The plunger actuators (29) drive the plunger (20) for the Fluid 1 syringe (19) or the plunger (36) for the Fluid 2 syringe (35). The syringes are moved perpendicular to the drive shaft axis by the switching mechanism (not shown) in order for either mechanical link (40) to be engaged to the drive shaft. The syringes (19) and (35) are fastened to the switching mechanism (not shown) through a pair of adjustable syringe clamps (30).

Fluid flows from either syringe through flexible fluid conduit

(42), to a valve (21), and through the needle adapter (26) to the needle (6). The pressure sensor (10) and flow sensor (not shown) monitor the flow at the distal end of the hand held assembly (housing not shown).

Once the needle tip is positioned at the desired point of action the flow of Fluid 1, the echogenic fluid, (19) is stopped to permit flow from Fluid 2, the therapeutic agent, (35). The fluid flow is switched by actuating a push button (22) connected to the switching mechanism (not shown). The switching mechanism (not shown) moves the syringes perpendicular to the drive shaft to simultaneously engage/disengage the links (40) to the syringe plunger actuators (29) and to switch the fluid flow through the valve (21) with a valve actuator (41).

Figure 4 depicts an isometric view of the switch mechanism and mechanical drive portion of the hand held assembly, configured to deliver drugs.

The syringe pump motor (16) is mechanically linked (39), to a drive shaft (37), which is supported by two bearings (38). The drive shaft is mechanically linked (40) to a syringe plunger actuator (29), which slides parallel to the drive shaft on the horizontal support rods of the switching mechanism (23), to actuate the syringe plunger (not shown). The syringe (not shown) is fastened to the switching mechanism (23) through an adjustable syringe clamp (30). Only one of the two sets of plunger actuators (29), links (40), and syringe clamps (30) are depicted in Figure 4.

The fluid flow is switched by actuating a push button (22) connected to the switching mechanism (23). The switching mechanism (23) moves the syringes perpendicular to the drive shaft to engage/disengage the link (40) between the syringe plunger actuator (29) and the drive shaft (37). The switching mechanism (23) also simultaneously switches the fluid flow through the valve (not shown) with a valve actuator (41).

Figures 5A and 5B depict top and side views of an embodiment of the invention using a mechanical mechanism to drive the fluid transfer.

A hand held assembly (5) with a needle adaptor (26) to hold a needle (6) for injecting drugs to a depth within a patient is shown. A pressure sensor (10) may be used to detect the fluid pressure. A top trigger control (12) is linked (not shown) to a mechanism (43) which pulses fluid from the Fluid 1 syringe (19). A lower trigger (13) is linked to a duplicate mechanism (43) which pulses fluid from the Fluid 2 syringe (35).

The mechanisms (43) consist of syringe plunger actuators (29), which clamp to the syringe plungers (20) and (36), drive springs (44), and control knobs (45) to adjust the pre-load tension of the springs (44). Such adjustment will vary the fluid flow of each pulse. The syringes (19) and (35) are fastened to the assembly (5) through a pair of adjustable syringe clamps (30).

Fluid flows from either syringe through conduit (42), to a mixing chamber (45), and through the needle adapter (26) to the needle (6).

An alternative embodiment of the mechanism (43) would be a mechanical peristaltic pump (not shown).

Figure 6 depicts an embodiment of the invention consisting of a hand held adapter connected to a commercial intravenous infusion pump.

A hand held assembly (5) with a needle adaptor (26) to hold a needle (6) for injecting drugs to a depth within a patient is shown. A pressure sensor (10) detects the fluid pressure. A trigger control (12) and switch (25) is used to switch the flow on and off. A flow adjustment knob (48) and sensor (not depicted) are used to vary the flow rate. The pressure sensor (10), flow adjustment sensor, and trigger switch (25) are connected via a wire wrap cable (27) to an electrical port (47), likely an RS232 port, on the commercial infusion pump (46).

The commercial infusion pump (46), such as a Baxter AS50, drives the fluid from the Fluid 1 syringe (19) through flexible fluid conduit (42) to the hand held assembly (5).

When the needle (6) is positioned at the desired point of action within a patient, fluid is delivered from the Fluid 2 syringe (35). The Fluid 2 syringe (35) may be mounted to the hand held assembly (5) or, as depicted in figure 6, the Fluid 2 syringe (35) may be held separately and manually actuated by attending health care personnel. The Fluid 2 syringe needle (49) pierces a port (50) in the hand held assembly and the fluid is ejected out of the syringe (35) and down through the hand held assembly needle (6) into the patient.

CONCLUSION

A medical device to inject drugs, drain bodily fluids, or to perform biopsy is disclosed. The device will permit localized drug delivery, fluid drainage, or biopsy through real-time monitoring of the needle tip position within a patient. The device will permit controlled dispersion of a drug into solid tissue as well as delivery into specific blood vessels.

The device is comprised of a handheld assembly with a needle, needle adapter, vessels to contain two different fluids, pump, controls, and may also be comprised of a pressure sensor, flow sensor, fluid switch mechanism, and valve. This assembly will likely be connected to a pressure meter, flow meter, controller, controller I/O, display, and power source.

As the needle is inserted, the first fluid, an echogenic suspension, possibly an ultrasonic contrast agent, is injected into the patient. The fluid travels a brief distance before being slowed and stopped by the patient's tissue. This speed and travel distance will be of sufficient magnitude as to be detectable by ultrasound, likely Doppler ultrasound, which is commonly used to image blood flow. The patient's internal organs can be displayed in grey-scale while the Doppler ultrasound assigns a distinct color to the fluid flow at the needle tip.

The health care personnel will monitor the position of the needle tip during insertion until said tip is positioned at the desired point of action, for instance a particular organ

or a cancer tumor. The second fluid, likely a therapeutic drug, is then delivered. Alternatively, a vacuum pump could then be used to aspirate tissue for biopsy or fluid for drainage.

During needle insertion, the first fluid may be pumped continuously or intermittently using the manual controls, or pulsed using the processor. The health care personnel will monitor the needle tip position through an ultrasound display and may adjust the fluid flow rate. This will vary the volume of space detectable by the ultrasound so as to maintain a properly defined image of the needle tip.

The device can also be used to precisely control the dispersion pattern of a delivered drug. Once the needle tip is positioned at the point of action, the health care personnel can pulse the echogenic fluid, repeatedly and at a variety of flow rates if necessary, and monitor the fluid distribution pattern. Once this is satisfactory, the second fluid, the therapeutic agent, can then be delivered.

The device may display the set flow rate, fluid pressure, and the rate of change of the pressure to the attending health care personnel. The pressure required to maintain a constant, set flow rate through a needle will vary as the back pressure varies due to the depth of insertion and changes in density of the patient's tissue, i.e. as the needle tip passes from fat to muscle. The back pressure may drop sharply if the needle tip pierces a blood vessel wall and the echogenic fluid is ejected directly into an artery or vein. Therefore, by monitoring the pressure and the rate of change of pressure,

the health care personnel will be able to position the needle to deliver drugs directly into a particular blood vessel. This could be advantageous for localized delivery of angiogenic drugs for heart conditions or, if the device is used to locate the artery that feeds a particular cancer tumor, for delivering anti-angiogenic drugs for cancer therapy.

The disclosed device combines existing technology and techniques:

- needles for drug delivery and biopsy
- -syringe pumps and vacuum pumps
- -ultrasound and Doppler ultrasound to image blood flow
- -commercially available components such as controllers, miniature electric motors, valves, pressure meters, and flow meters
- ultrasound contrast agents

The foregoing has constituted a description of specific embodiments showing how the invention may be applied and put into use. These embodiments are only exemplary. The invention in its broadest, and more specific aspects, is further described and defined in the claims which now follow.

These claims, and the language used therein, are to be understood in terms of the variants of the invention which have been described. They are not to be restricted to such variants, but are to be read as covering the full scope of the invention as is implicit within the invention and the disclosure that has been provided herein.

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A device comprising:

a) a needle for insertion into a patient,

b) fluid supply means to supply to the needle fluid to be ejected out the distal end of the needle where it may travel a brief distance before being slowed and stopped by the patient's tissue, said fluid supply means delivering fluid at a fluid flow rate that is sufficient to render the ejected fluid to be detectable by ultrasound.

c) Doppler or other types of ultrasound motion detection means positioned to identify the location of the ejected fluid before it is slowed and stopped by the patient's tissue, and

d) display means coupled to the ultrasound motion detection means to provide an indication of the location of the ejected fluid so detected.

2. A device as described in claim 1 wherein the fluid supply means supplies a pulsed, continuous, or intermittent fluid flow.

3. A device as described in claims 1 or 2 in combination with a controller processor coupled to the fluid supply means whereby the fluid flow rate can be adjusted in real-time

during needle insertion, in conjunction with the real-time monitoring of the needle position using the ultrasound, in order to maintain a relatively small volume of flowing fluid in proximity to the needle tip.

4. A device as described in claims 1, 2, and 3 with a second fluid supply means to supply fluid to be ejected out of the distal end of the needle. Once the needle is positioned at the desired point of action this second fluid, likely a therapeutic agent, will be ejected as shown in figure 1, and hence permit localized drug delivery.

5. A therapeutic agent as described in claim 4 may be a liquid drug, solid drug particles suspended in a fluid, drug eluting microspheres suspended in a fluid, radioisotope labelled drugs or microspheres, or other therapeutic agents that can be delivered under pressure through a needle. A PortaCath type flexible conduit, Hickman line, or PICC may be inserted into the needle and the needle removed in order to provide access for repeat dosage drug delivery. A radiolabelled rod may be inserted down through the needle to provide brachytherpy type treatment. An imaging system contrast agent, such as but not limited to contrast agents for CT scan, MRI, or X-ray, may also be delivered.

6. A device as described in claims 1, 2, and 3 in combination with a vacuum source. Once the needle is positioned at the desired point of action, a vacuum source may be used to aspirate tissue for biopsy or to drain fluid as shown in figure 2. A stylet may be used with the needle in order to perform biopsy.

7. A fluid supply means for said device as described in claims 1, 2, 3, and 4 comprising:

a) a pumping mechanism and fluid vessels, and may also contain a flow meter,

b) an embodiment of this fluid supply means comprised of a syringe

c) pump driving either of two syringe plungers, with a flow meter transducer, positioned at the distal end of the hand held assembly, to sense the flow rate, as depicted in figure 3

d) an embodiment of this fluid supply means comprised of a separate syringe pump for both syringes and/or a flow meter transducer that senses the position and speed of the plungers and/or a microprocessor incorporated in the hand held assembly

e) an embodiment of this fluid supply means comprised of a variable speed fluid transfer pump connected to ampules or capsules incorporated in the hand held assembly.

8. An embodiment of the device as described in claims 1, 2, and 4 whereby the fluid transfer system is comprised of a syringe pump and syringes and the fluid switch system is as depicted in figures 3, 3A, and 4, such that:

syringes for two fluids are contained within the hand held assembly in a sliding base with adjustable clamps

the syringe plungers are driven by syringe plunger

actuators, which slide on horizontal support rods

an electric motor, such as a miniature stepper motor, is linked to a drive shaft which is positioned parallel to the two syringes

the motor rotates the drive shaft in order to engage either plunger

a sliding mechanism will operatively engage either syringe plunge actuator to the drive screw

the motor is actuated by a processor, possibly with a stepper motor driver card, linked to the manual controls

flow through the needle is switched from Fluid 1 to Fluid 2 using a valve and flexible fluid conduit

a mechanism to switch from Fluid 1 to Fluid 2 is comprised of a push button that moves the switch mechanism frame perpendicular to the drive shift; this movement simultaneously switches the fluid valve and syringe plunger actuators; therefore the device cannot inadvertently be set to pump fluid from a syringe whose fluid flow valve is shut.

9. A drug delivery device as described in claims 1, 2, 4, and 5 capable of

precise control of the volume of drug delivered, using the flow meter, controller, and pump

precise control of the dispersion pattern of a delivered therapeutic agent. Once the needle tip is positioned at the point of action, the first fluid (an echogenic fluid which may be sterile saline or an ultrasound contrast agent or other suitable fluids) can be delivered, repeatedly and at a variety of flow rates if necessary, and the fluid distribution pattern monitored using the ultrasound display. Once said pattern is satisfactory, the second fluid, the therapeutic agent, can then be delivered.

10. A drug delivery device as described in claims 1, 2, 4, 5, and 6, and as shown in figures 3 and 3A, whereby

a variety of needle sizes can be fitted to the device through a leak-proof adapter, likely a threaded adapter

a variety of needle tip geometries may be fitted to the device, including a standard open end, an angled open end, or a closed end with slots running along the side of the needle tip, or combinations of the above the fluid vessels (syringes or ampules) are held in the device with adjustable clamps and connected to flexible fluid conduits using leak proof fittings such as Luer™ locks

the injectate contacting surfaces of the device - syringes, valves, needle, needle adapter, conduits, and fittings - are accessible through a removable cover and replaceable in order to maintain the sterility of said components for each injection

the manual flow rate control is comprised of a trigger and positional sensor

the flow rate on/off control is comprised of a trigger and a switch

the pressure sensor is located at the distal end of the hand held assembly

the flow sensor is located at the distal end of the hand held assembly

the pressure meter, flow meter, controller, and display for the flow meter and pressure meters are stationed on a convenient platform(s), and connected to the hand held assembly through wire wrap cabling.

11. A drug delivery device as described in claims 1, 2, 4, 5, 6, and 7 whereby

the real-time flow rate, fluid pressure, and the rate of change of the fluid pressure, may be displayed to the attending health care personnel as shown in figure 1

as the pump pressure required to maintain a steady flow rate may drop sharply if the needle tip pierces a blood vessel wall and the echogenic fluid is ejected directly into an artery or vein, the health care personnel will be able to position the needle to deliver drugs directly into a particular blood vessel using the pressure and rate of change of pressure display.

12. A biopsy or fluid drainage device as described in claim 3 whereby:

the real-time flow rate, fluid pressure, rate of change of the fluid pressure, and vacuum may be displayed to the attending health care personnel as shown in figure 2.

13. An embodiment of the device as described in claims 1,2,4,5, and 6 whereby the fluid transfer system is comprised of a mechanical syringe pump and syringes and a fluid mixing system as depicted in figure 5A and 5B such that:

syringes for two fluids are contained within the hand held assembly in a sliding base with adjustable clamps

the syringe plungers are driven by syringe plunger actuators, which slide on horizontal support rods

a mechanical means to drive the plungers, such as a spring loaded system depicted in figure 5A and 5B, is positioned parallel to the two syringes

the spring loads may be adjusted to vary the fluid pulse flow rate

flow through the needle is switched from Fluid 1 to Fluid 2 by actuating either syringe plunger and driving the fluid through a mixing chamber and into the needle

a mechanism to switch from Fluid 1 to Fluid 2 may be used

as described in claim 5

a mechanical peristaltic pump system or other mechanical pumping methods may alternatively be used to drive the fluid instead of the spring mechanism depicted in figure 5A and 5B.

14. An embodiment of the device as described in claims 1, 2, 4, 5, and 6 whereby the fluid transfer system is comprised of a hand held adaptor that actuates a commercial intravenous infusion pump, such as a Baxter AS50, as depicted in figure 6, such that:

a syringe for the first fluid, the echogenic suspension, is clamped in a sliding base to the commercial infusion pump which drives the fluid through conduit to the hand held adapter

a syringe for the second fluid, the therapeutic agent, may be clamped to a second commercial infusion pump and connected to the hand held adapter via fluid conduit, or it may be clamped to the hand held adapter and acutated manually or with mechanical assistance, or it may be an independent needle and syringe as depicted in figure 6; the independent needle and syringe can be used to eject fluid into a port on the hand held assembly in order to deliver the therapeutic agent into the patient

controls on the hand held assembly, and a microprocessor controller, will likely connect to the commercial infusion pump through an RS232 port, and will be used to

drive the infusion pump

the controls may be used for continuous or pulsed flow with an adjustable flow rate

flow through the needle is switched from Fluid 1 to Fluid 2 by actuating either syringe plunger and driving the fluid through a mixing chamber and into the needle.

15. A drug delivery device as described in claims 1, 2, 3, 4, and 5 capable of

injecting gas filled microspheres to a depth within a patient that, under external ultrasound, rupture to release a therapeutic compound

delivering a rupturing ultrasound pulse down through the needle from a transducer, power, and control system mounted in the syringe.

16. An embodiment of the device as described in claims 1, 2, 3, 4, 5, and 6 whereby the needle to be inserted into the patient is comprised of:

a multiple lumen, likely a double lumen

the fluid transfer flow is configured such that fluid 1 and fluid 2 do not mix prior to injection into the patient and that each fluid transferred down a separate lumen into the patient

a stylet may be incorporated into the multiple lumen for biopsy or fluid drainage use; the stylet would prevent tissue ingress into the lumen intended to aspirate tissue while the lumen for injecting fluid 1 remained open.

17. An embodiment of the device as described in claims 1, 2, 3, 4, 5, and 6 whereby the device is adapted to deliver fluid into a catheter in order to deliver fluids into a patient.

The pressure required to maintain a constant flow rate through a needle likely changes if the needle pierces a blood vessel wall and the echogenic fluid is ejected directly into an artery or vein. By monitoring the pressure and the rate of change of pressure, the needle can be positioned to deliver drugs directly into a particular blood vessel.

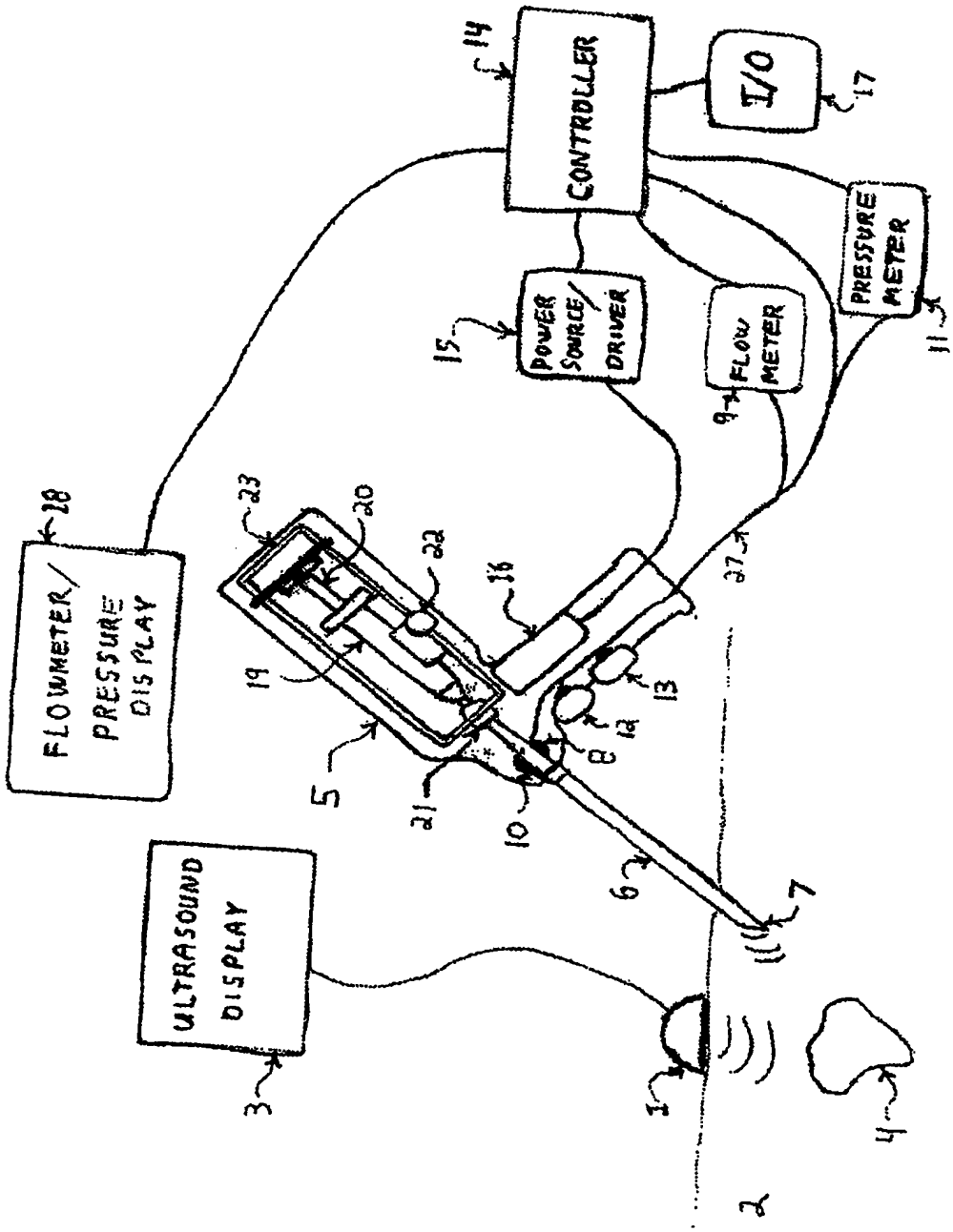

CONTROLLER
I/O
POWER SOURCE/ DRIVER
FLOW METER
PRESSURE METER
FLOWMETER/ PRESSURE DISPLAY
ULTRASOUND DISPLAY
DRUG DELIVERY

FIGURE 1

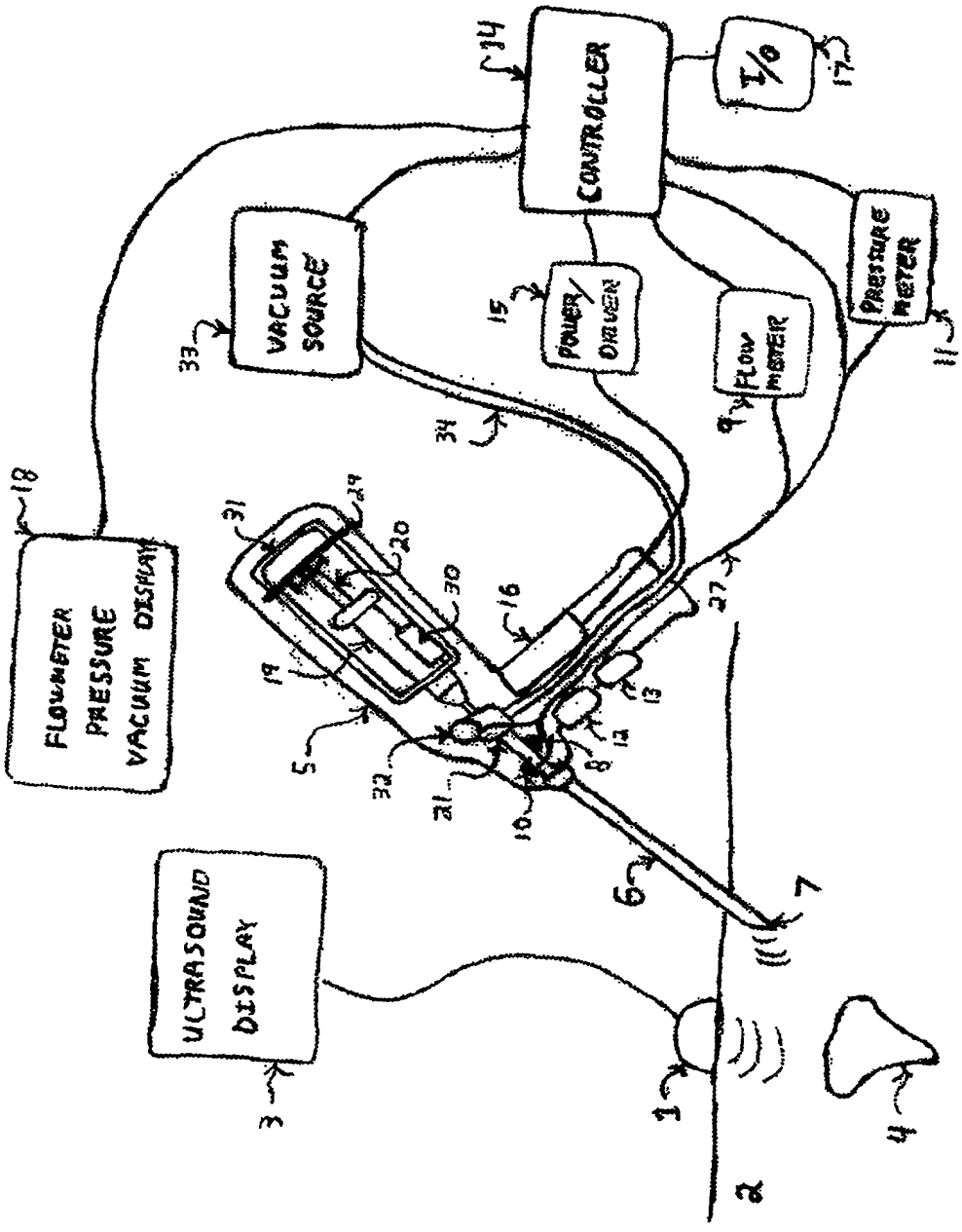

FLOWMETER
PRESSURE
VACUUM DISPLAY
18
ULTRASOUND
DISPLAY
3
VACUUM
SOURCE
33
34
CONTROLLER
14
I/O
17
POWER/
DRIVER
15
FLOW
METER
9
PRESSURE
METER
11
BIOPSY
1
2
4
5
6
7
8
10
12
13
16
19
20
21
27
29
30
31
32

FIGURE 2

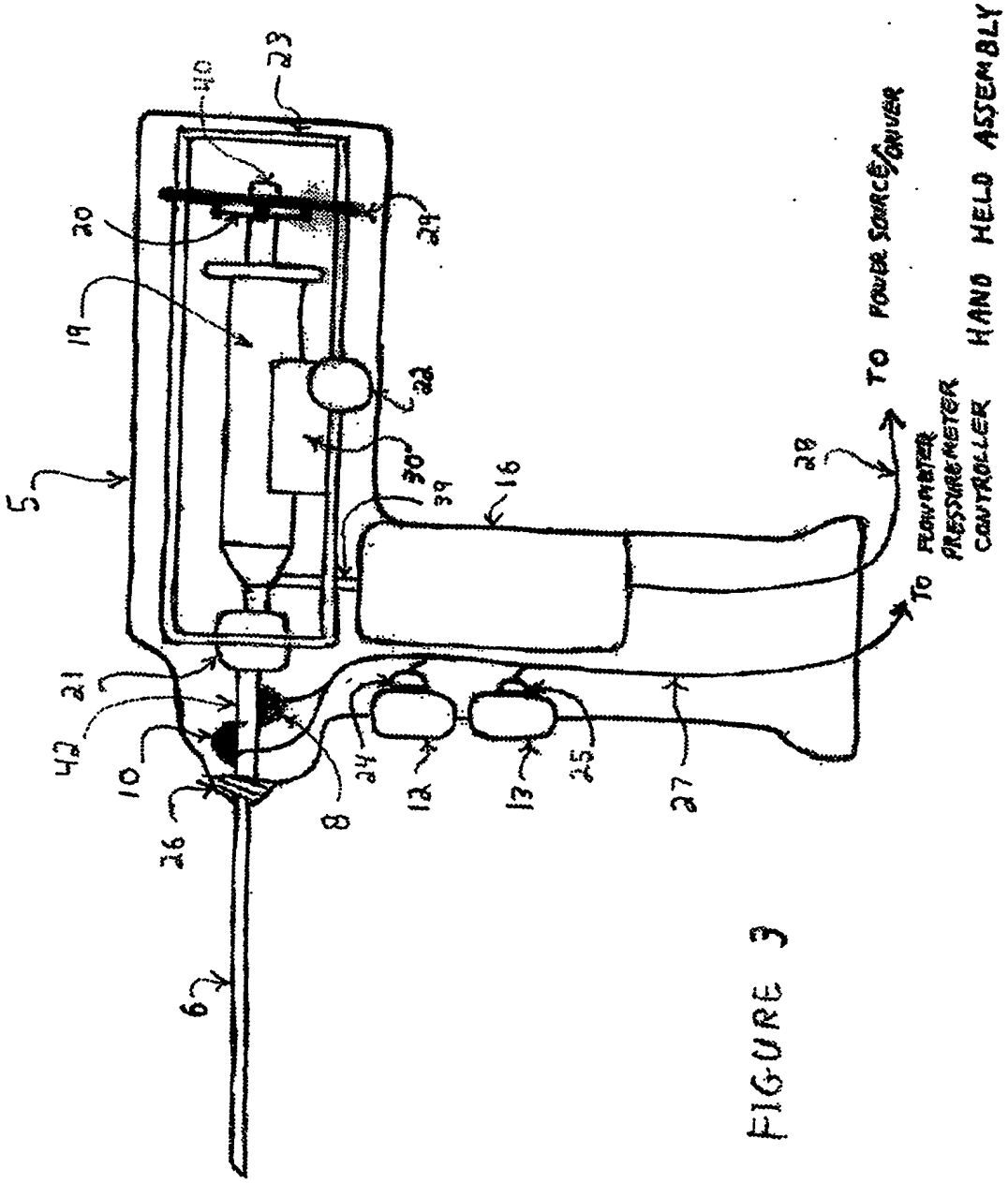

40
23
20
29
19
22
30
39
16
5
28
TO POWER SOURCE/DRIVER
TO FLOWMETER PRESSUREMETER CONTROLLER
HAND HELD ASSEMBLY
21
42
10
24
12
13
25
27
8
26
6

FIGURE 3

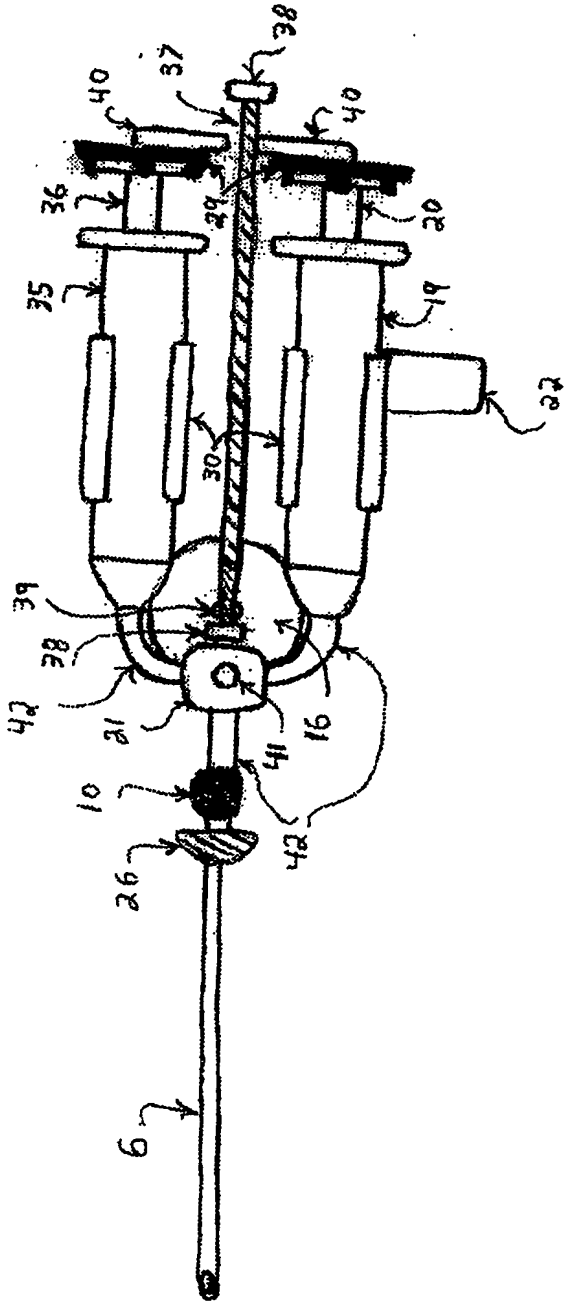


FIGURE 3A

TOP VIEW

FLUID FLOW + DRIVE

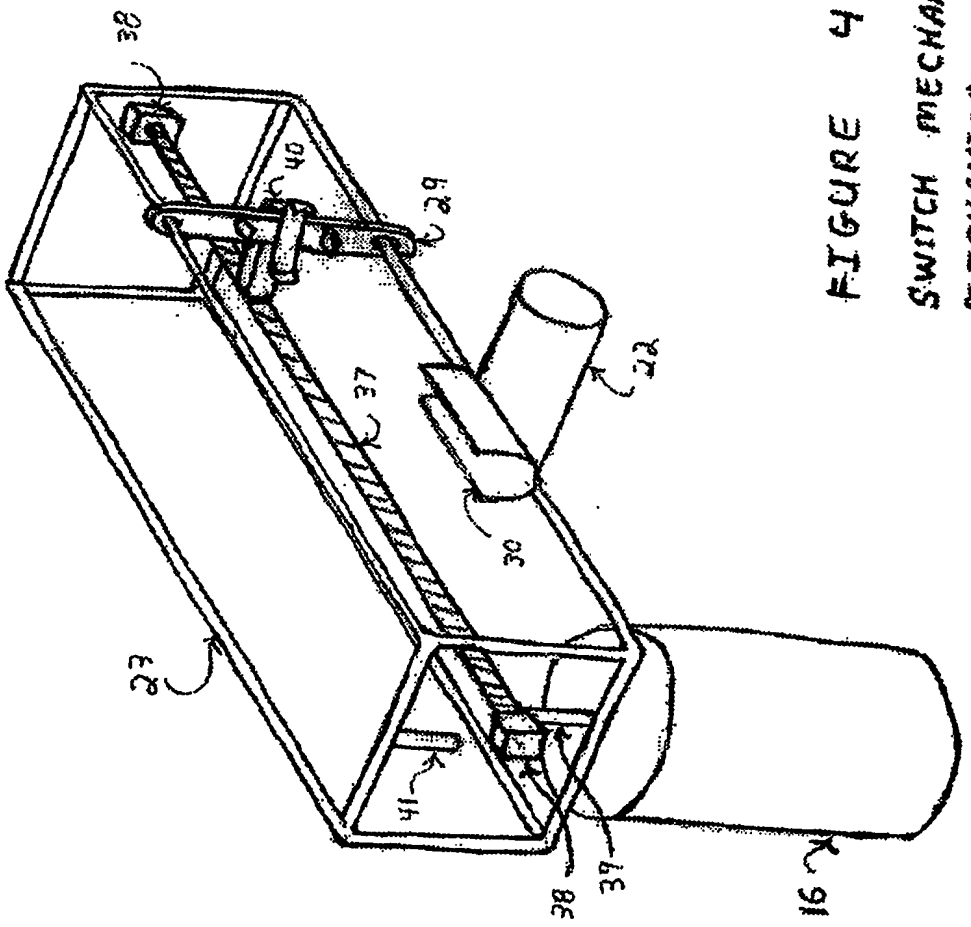


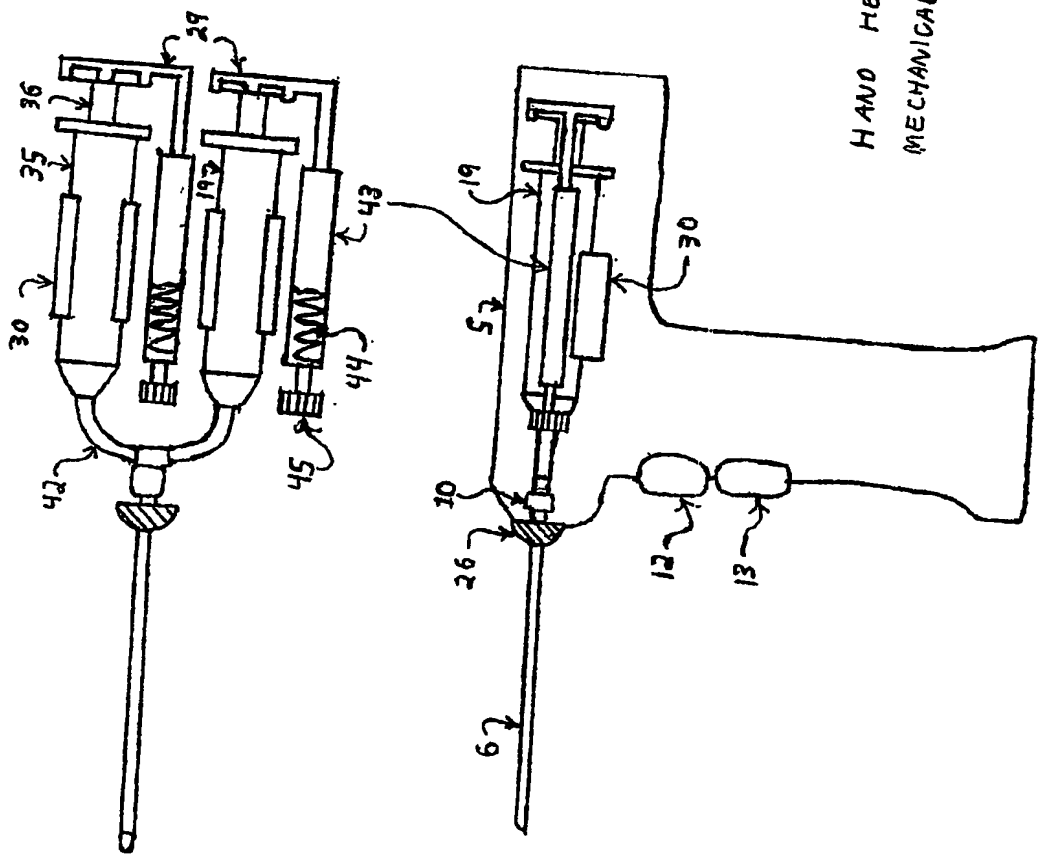
FIGURE 4

SWITCH MECHANISM + MECHANICAL DRIVE

HAND HELD ASSEMBLY
MECHANICAL EMBODIMENT

FIGURE 5B
SIDE VIEW

FIGURE 5A
TOP VIEW



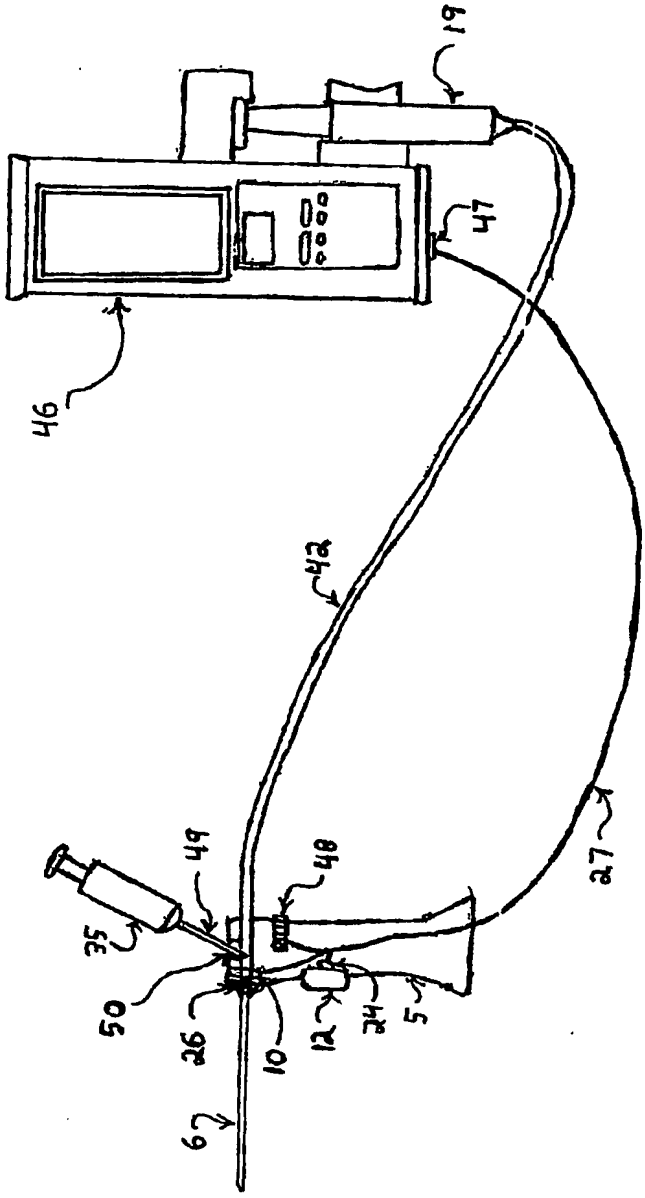


FIGURE 6 INFUSION PUMP ADAPTOR